Journal of BUON **8:** 389-392, 2003

CLINICAL CASE

The effect of epithelial and myoepithelial differentiations on survival in a parotid gland undifferentiated carcinoma: case report and review of the literature

G. Aksu[1], A. Karadeniz[2], M. Fayda[2], F. Dizdaroglu[3]

[1]Italian Hospital, Radiotherapy Department; [2]Istanbul University, Institute of Oncology, Radiotherapy Department; [3]Istanbul University, Istanbul Medical Faculty, Pathology Department, Istanbul, Turkey

Summary

Undifferentiated carcinoma of the parotid gland is a rare tumor, with an incidence of 5-10% among all parotid tumors. Salivary gland tumors frequently present myoepithelial cell differentiation. Recognition of myoepithelial cell differentiation is not easily apparent on routinely stained sections and it often requires immunohistochemical or ultrastructural studies. The relationship between these differentiations and survival is still not clear. We report on a 71-year-old male with left parotid undifferentiated small cell carcinoma with epithelial and myoepithelial differentiation that relapsed at the parotid region and neck nodes 4 years after he had undergone superficial parotidectomy. The relapsing disease was treated with total parotidectomy and radical left neck dissection. Also, postoperative radiotherapy was given to the left parotid region and the neck. In total, he is alive 8.5 years from the beginning of the disease, and 54 months after the second surgery and radiotherapy. No disease recurrence has occurred ever since. Undifferentiated carcinomas with epithelial and myoepithelial differentiation are rarely seen and differential diagnosis should be made with salivary gland myoepitheliomas and epithelial-myoepithelial carcinomas. Better understanding of the impact of these differentiations on survival will come with the evaluation of more cases of this unusual malignancy.

Key words: epithelial and myoepithelial differentiation, parotid cancer, radiotherapy, undifferentiated carcinoma

Introduction

Undifferentiated carcinoma of the parotid gland is a very rare tumor, representing about 5-10% of all parotid tumors [1-5]. The diagnosis is made by the presence of undifferentiated tumor cells under light microscopic examination. This tumor is encountered in older ages compared to other parotid gland tumors, and has the worse prognosis among them [6,7]. Salivary gland tumors frequently present myoepithelial cell differentiation which is not always easily identified on routinely stained sections. Undifferentiated carcinomas with epithelial and myoepithelial differentiation are rarely seen, and differential diagnosis should be made with salivary gland myoepitheliomas and epithelial-myoepithelial carcinomas.

In this communication we present a patient with parotid small cell undifferentiated carcinoma with epithelial and myoepithelial differentiation and discuss the differential diagnosis and the impact of tumors of such histology on survival by reviewing the recent relevant literature.

Received 25-07-2003; Accepted 14-08-2003

Author and address for correspondence:

Gorkem Aksu, MD
Italian Hospital
Radiotherapy Department
Defterdar Yokuşu No: 37
Tophane
Istanbul
Turkey
Tel: + 90 212 292 90 00, ext : 2013
Fax: + 90 212 292 84 38
E-mail: aksugorkem@yahoo.com

Case presentation

A 71-year-old man was referred for radiotherapy after total parotidectomy and left radical neck

dissection. Five years ago he had noticed a mass anteriorly to his left ear. The mass had grown up for a year and then he underwent a superficial left parotidectomy in another hospital. After a 4-year follow up a mass appeared, measuring 3×3 cm in front of the tragus under the scar of the previous operation; there was also a 3×2 cm palpable node in the upper jugular region of the left neck. There was no facial nerve palsy. The patient had diabetes mellitus for 6 years which was under control with oral treatment. Computed tomographic scans of the chest and whole abdomen were normal.

A radical parotidectomy with full-thickness excision of the skin, radical left neck dissection and reconstruction with pectoralis major myocutaneous flap was carried out. Macroscopically, a yellow-brownish tumor measuring 2.5×2×3 cm was found in the left parotid invading the overlying soft tissues and skin. Microscopically the tumor cells had small, uniform and round nuclei and small cytoplasm. The epithelial cells were columnar with atypical round nuclei, prominent nucleoli and eosinophilic cytoplasm (Figure 1). Perineural invasions were seen among the nerves in the tumor region (Figure 2). Immunohistochemical examination was made to evaluate neuroendocrine, epithelial, myoepithelial differentiation or lymphoid origin of the tumor. The tumor cells stained weakly for vimentin and focally weakly for pancytokeratin (Figures 3 and 4). They also stained positively for smooth muscle actin and calponin. The histopathological findings were consistent with an undifferentiated carcinoma with epithelial and myoepithelial differentiation of the parotid gland.

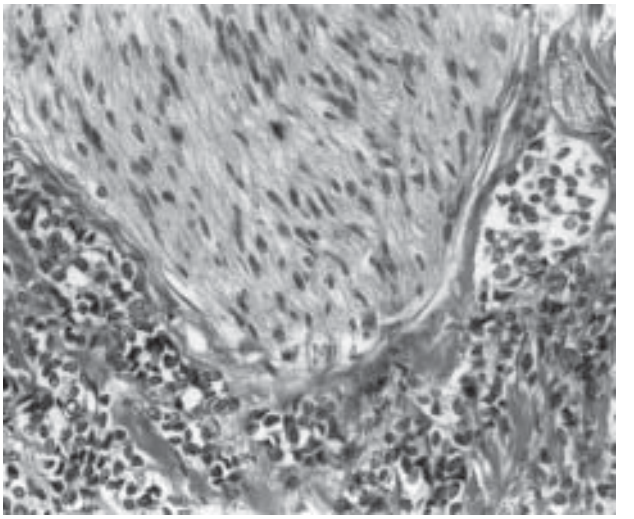

Figure 2. Region of perineural invasion (H&E ×250).

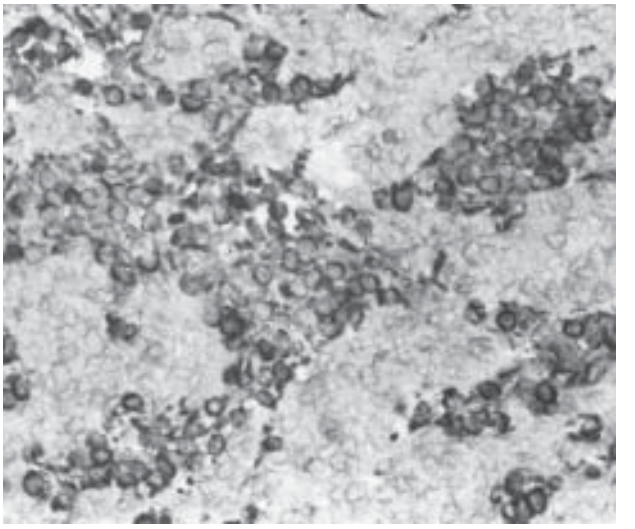

Figure 3. Tumor cells positively stained for vimentine (×400).

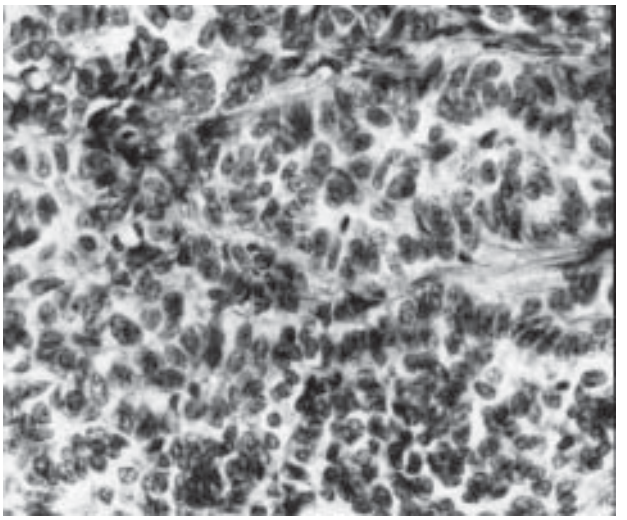

Figure 1. Undifferentiated tumor of the parotid gland (H&E ×400).

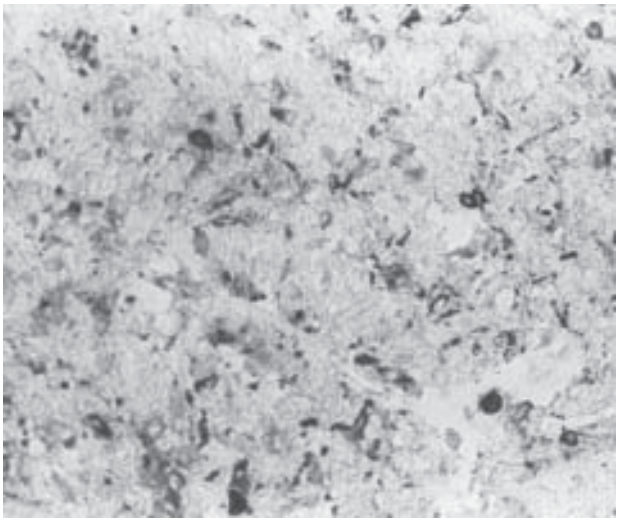

Figure 4. Tumor cells with weakly positive staining for pancytokeratin (×400).

Three of 17 lymph nodes showed metastatic deposits from undifferentiated carcinoma. The pathological stage was T2N2bMx.

The patient was given postoperative adjuvant radiotherapy with total dose of 60 Gy in 30 fractions, 5 fractions weekly, using cobalt 60 to the left parotid and neck region.

He lives disease-free 54 months after radiotherapy. The only finding in the routine magnetic resonance imaging of the parotid and the neck is the heterogeneity of the soft tissue in the operation region due to surgery and radiotherapy.

Discussion

Undifferentiated carcinoma of the salivary glands is a malignant tumor of epithelial structure but can't be placed in any group of the other carcinomas because of not having enough distinguishing phenotypic features by light microscopy [5,8]. Its incidence varies from 1 to 20% in different studies [7]. The major reason of this difference is the presence of highly anaplastic and undifferentiated epithelial cells. Also, metastases from Merkel cell carcinomas, nasopharyngeal carcinomas or amelanotic melanomas can be additional reasons for misclassification [9]. Literature data show a dismal prognosis of undifferentiated carcinoma of the salivary glands. In a recent study of survival by Wahlberg et al., the incidence of undifferentiated carcinoma of the parotid among the different parotid malignancies was found to be 10% and 5 and 10-year overall survival rates were 48% and 44%, respectively [5]. In another study Garden et al. found an incidence of undifferentiated carcinoma of only 2% [10]. North et al. pointed out that undifferentiated histology was associated with decreased survival [11]. Terhaard et al. mentioned that the risk of distant metastases was higher among the patients with undifferentiated histology. They reported a 7% incidence of undifferentiated carcinoma of the parotid and stated that poor differentiation raised the risk of distant metastases [12]. Poulsen et al. also reported that poor differentiation is one of the major bad prognostic variables [13].

Salivary gland tumors frequently present myoepithelial cell differentiation that is not always easily identified on routinely stained sections. Epithelial and myoepithelial differentiation in an undifferentiated carcinoma has been described recently due to improvements in immunohistochemistry. Markers such as calponin (CALP), caldesmon (CALD), and smooth muscle myosin heavy chain, together with smooth muscle actin may be useful tools for identifying myoepithelial cells. Among the 4 markers studied, CALP and smooth muscle actin were the most useful in identifying myoepithelial cell differentiation [14].

In a recent study, among 7 immunohistochemical markers tested, antibodies against cytokeratins 5/6, S-100 protein, and vimentin produced the most consistent reactivity profile [15]. In our case, tumor cells stained weakly for vimentin and focally weakly for pancytokeratin, smooth muscle actin and CALP.

Myoepitheliomas, epithelial-myoepithelial carcinomas, pleomorphic adenomas and Merkel cell carcinomas should be considered in differential diagnosis. Myoepithelioma, a rare benign salivary gland neoplasm, is a tumor composed entirely of myoepithelial cells. Unlike pleomorphic adenoma, these tumors lack any ductal epithelial differentiation, and manifest a minor stromal element. The varying growth patterns and the chondromyxoid areas seen in pleomorphic adenoma are not seen in undifferentiated carcinoma. In epithelial-myoepithelial carcinomas, the tumor is thought to originate from the intercalated duct cells. It usually develops in the parotid gland of the women between 70-80 years of age. The prognosis is generally good and it is believed that in a mixed tumor epithelial and mesenchymal components retain their own characteristics [16]. In many cases it is easy to determine myoepithelial cells which are rich in glycogen and stain with periodic acid-Schiff. Since epithelial-myoepithelial carcinomas generally have a good prognosis, it is thought that undifferentiated carcinomas with epithelial and myoepithelial differentiation have better prognosis than those without differentiation, but yet data are not enough to be sure of.

Today most of the oncologists agree that total parotidectomy and neck dissection is the proper treatment for the undifferentiated carcinomas of the parotid since they are high grade tumors and tend to relapse locally and also to develop distant metastases [2,5,11,17]. Superficial parotidectomy without neck dissection, like in our case, can be performed only for low grade tumors such as mucoepidermoid carcinoma and acinic carcinomas with minimal invasion.

Postoperative radiotherapy is also standard treatment for parotid gland undifferentiated carcinomas. Local and regional control rates were higher for patients with high grade parotid tumors such as undifferentiated carcinomas who had postoperative radiotherapy. Most authors agree that 60 Gy in 30 fractions with electron beam should be given to the parotid gland and involved neck [2,5,10-13].

Although our patient had relapse of the primary cancer with nodal metastases 4 years after the pri-

mary surgery, he is still alive without evidence of disease 4.5 years post-relapse with radical surgery and postoperative radiotherapy.

In conclusion, undifferentiated carcinomas with epithelial and myoepithelial differentiation seem to be related with better prognosis than those without these differentiations, and we believe that the importance of the presence of epithelial and myoepithelial component as a prognostic factor for better local control and survival will be confirmed as the number of such reported cases increases. Overall, appropriate surgery, postoperative radiotherapy and long-term follow-up are the most important factors for better disease outcome and increased survival.

References

1. Simpson JR, Lee HK. Salivary Glands. In: Perez CA, Brady LW (eds). Principles and Practice of Radiation Oncology (3rd edn). Lippincott-Raven Publ, Philadelphia, New York, 1998, pp 961-980.
2. Soni SC, Kahn FR, Paul JM et al. Electron beam treatment of malignant tumours of the salivary glands. J Radiol Electrol Med Nucl 1997; 58: 677-679.
3. Fang B, Forastiere A. Head and Neck. In: Abraham J, Allegra CJ (eds). Bethesda Handbook of Clinical Oncology (1st edn). Lippincott Williams & Wilkins, Philadelphia, 2001, pp 3-30.
4. Foote FW, Frazell EL. Tumors of the major salivary glands. Armed Forces Institute of Pathology, Washington DC, 1954.
5. Wahlberg P, Anderson H, Biörklund A, Möller T, Perfekt R .Carcinoma of the parotid and submandibular glands- a study of survival in 2645 patients. Oral Oncol 2002; 38: 706-713.
6. Östman J, Anneroth G, Gustafsson H, Tavalin B .Malignant salivary gland tumours in Sweden 1960-1989 an epidemiological study. Oral Oncol 1997; 33: 169-176.
7. Ellis GL, Auclair PL. Tumours of the salivary glands. Armed Forces Institute of Pathology, Washington DC, 1996.
8. Seifert G, Sobin LH. The World Health Organisation's histological classification of tumours. A commentary on the second edition. Cancer 1992; 70: 379-385.
9. Hui KK, Luna MA, Batsakis JG, Ordonez NG, Weber R. Undifferentiated carcinomas of the major salivary glands. Oral Surg Oral Med Oral Path 1990; 69: 76-83.
10. Garden AS, El-Naggar AK, Morrison WH, Callender DL, Ang KK, Peters LJ. Postoperative radiotherapy for malignant tumours of the parotid gland. Int J Radiat Oncol Biol Phys 1997; 37: 79-85.
11. North CA, Lee DJ, Piantadosi S, Zahurak M, Johns ME . Carcinoma of the major salivary glands treated by surgery or surgery plus radiotherapy. Int J Radiat Oncol Biol Phys 1990; 18:1319-1326.
12. Terhaard CHJ, Lubsen H, van der Tweel I, Hilgers FJM, Eijkenboom WMH. Salivary gland carcinomas: Prognostic factors for local control and distant metastases: The role of radiotherapy. Int J Radiat Oncol Biol Phys 1997; 39 (Suppl 1): 189 (abstr #2).
13. Poulsen MG, Pratt GR, Kynaston B, Tripcony LB. Prognostic variables in malignant epithelial tumours of the parotid. Int J Radiat Oncol Biol Phys 1992; 23: 327-332.
14. Scarpellini F, Marucci G, Foschini MP. Myoepithelial differentiation markers in salivary gland neoplasia. Pathologica 2001; 93: 662-667.
15. Hungermann D, Roeser K, Buerger H, Jakel T, Loning T, Herbst H. Relative paucity of gross genetic alterations in myoepitheliomas and myoepithelial carcinomas of salivary glands. J Pathol 2002; 198: 487-494.
16. Corio RL, Sciubba JJ, Brannon RB, Batsakis JG. Epithelial-myoepithelial carcinoma of intercalated duct origin. A clinicopathologic and ultrastructural assessment of sixteen cases. Oral Surg Oral Med Oral Pathol 1982; 53:280-287.
17. Blanck C, Backström A, Eneroth CM, Jakobsson PA. Poorly differentiated solid parotid carcinoma. Acta Radiol Ther Phys Biol 1974; 13: 17-31.